(FILE 'HOME' ENTERED AT 15:35:47 ON 28 MAR 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 15:35:59 ON 28 MAR 2003

L1 4039579 S TUMOR OR NEOPLAS? OR TUMOUR OR CANCER?
L2 657617 S L1 AND (CULTUR? OR ASSAY OR IN(W)VITRO)
L3 27534 S L2 AND (INVASION OR MIGRATION OR OUTGROWTH)
L4 5763 S L3 AND INHIBITION
L5 5763 FOCUS L4 1-
L6 429 S L4 AND INTEGRIN
L7 230 DUP REM L6 (199 DUPLICATES REMOVED)
L8 230 FOCUS L7 1-

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L5 ANSWER 8 OF 5763 CAPLUS COPYRIGHT 2003 ACS
AN 1999:691229 CAPLUS
DN 131:317761
TI **Inhibition** of **tumor invasion** or spreading based on a soluble receptor for advanced glycation endproducts
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
IN Schmidt, Ann Marie; Stern, David
AB The present invention provides for a method for inhibiting **tumor invasion** or metastasis in a subject which comprises administering to the subject a therapeutically effective amt. of a form of sol. receptor for advanced glycation endproducts (RAGE). Interruption of cellular RAGE-extracellular matrix (amphoterin and/or similar structures) interaction appears to be at least one mechanism by which sRAGE limits **tumor** growth. The present invention also provides a method for evaluating the ability of an agent to inhibit **tumor invasion** in a local cellular environment which comprises: (a) admixing with cell **culture** media an effective amt. of the agent; (b) contacting a **tumor** cell in cell **culture** with the media from step (a); (c) detg. the amt. of spreading of the **tumor** cell **culture**, and (d) comparing the amt. of spreading of the **tumor** cell **culture** detd. in step (c) with the amt. detd. in the absence of the agent, thus evaluating the ability of the agent to inhibit **tumor invasion** in the local cellular environment. The present invention also provides a pharmaceutical compn. which comprises a therapeutically effective amt. of the agent evaluated in the aforementioned method and a pharmaceutically acceptable carrier.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9954485	A1	19991028	WO 1999-US8427	19990416
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6465422	B1	20021015	US 1998-62365	19980417
CA 2325573	AA	19991028	CA 1999-2325573	19990416
AU 9934957	A1	19991108	AU 1999-34957	19990416
EP 1071794	A1	20010131	EP 1999-916699	19990416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002512038	T2	20020423	JP 2000-544814	19990416
US 2002177550	A1	20021128	US 2001-851071	20010508

L5 ANSWER 1 OF 5763 CAPLUS COPYRIGHT 2003 ACS
AN 1985:94115 CAPLUS
DN 102:94115
TI In vitro **migration** of **tumor** cells from human **neoplasms**: **inhibition** by lymphokines
SO Clinical Immunology and Immunopathology (1985), 34(1), 94-9
CODEN: CLIIAT; ISSN: 0090-1229

AU Cohen, Marion C.; Forouhar, Faripour; Donskoy, Mark; Cohen, Stanley
AB A noncytotoxic lymphokine, **tumor migration inhibition** factor (TMIF), with the capacity of inhibiting the in vitro **migration** of a variety of serially passaged exptl. animal **tumors**, but not non-**neoplastic** cells, was previously described. In the present study, conditions for the **assay** of human **tumor** cell movement utilizing agarose microdroplets is described. Using this procedure, it was demonstrated that TMIF is as effective in inhibiting the in vitro **migration** of suspensions of **tumor** cells obtained from spontaneous human **neoplasms**, as it is in inhibiting model **tumor** systems. Thus, responsiveness to TMIF is not merely a property conferred on **tumor** cells by prior serial passage. In addn., by demonstrating that **tumors** of human origin are responsive, the present study raises the possibility that studies of TMIF in **neoplastic** disease may provide information of prognostic value. Also, they provide the hope that if TMIF proves therapeutically effective in animal models, those results may be translated to human disease.

L5 ANSWER 4 OF 5763 CAPLUS COPYRIGHT 2003 ACS
AN 1997:272273 CAPLUS
DN 126:324869
TI A modified and convenient method for assessing **tumor** cell **invasion** and **migration** and its application to screening for inhibitors
SO Biological & Pharmaceutical Bulletin (1997), 20(4), 345-348
CODEN: BPBLEO; ISSN: 0918-6158
AU Saito, Ken-Ichi; Oku, Tohru; Ata, Naomi; Miyashiro, Hirotsugu; Hattori, Masao; Saiki, Ikuo
AB In order to screen potent inhibitors of **tumor invasion** and metastasis, we here devised a simple and reproducible in vitro **assay** for **tumor invasion** and **migration** . A conventional cell-counting **assay** using a Transwell chamber with a microporous membrane filter is troublesome and time-consuming, involving visually counting the cells under a microscope, and the invaded or migrated cells are sometimes distributed unevenly in predetd. fields on the lower surface of the filter. Therefore, it is difficult to evaluate the invasive and migratory abilities of **tumor** cells easily and quant. by the cell counting method. In the present study, crystal violet dye was used for staining the invaded cells and colorimetrically assessing the invasive ability per filter as an absorbance. In this crystal violet **assay**, **tumor** cell **invasion** into a reconstituted basement membrane Matrigel was proportional to both the cell no. added into the chamber and the incubation period, and inversely proportional to the amt. of Matrigel barrier on the upper surface of filter. The results obtained by this dye-uptake method were highly consistent with those of a conventional cell-counting **assay**. Using this crystal violet **assay**, the anti-invasive effect of doxorubicin (DOX) was detected more easily and found to be highly proportional to that by the conventional cell-counting method. We therefore applied this convenient **assay** method to screen anti-invasive and anti-metastatic compds. As a result, caffeic acid was found to be more active in the **inhibition** of both **tumor** cell **invasion** and **migration** without showing direct cytotoxicity in vitro than other related compds.

L5 ANSWER 5 OF 5763 CAPLUS COPYRIGHT 2003 ACS
AN 1994:400349 CAPLUS
DN 121:349
TI **Inhibition** of **tumor** cell **invasion** in the Boyden chamber **assay** by a mannosidase inhibitor, mannostatin A
SO Anticancer Research (1993), 13(5A), 1421-4
CODEN: ANTRD4; ISSN: 0250-7005
AU Ochi, Yusuke; Atsumi, Sonoko; Aoyagi, Takaaki; Umezawa, Kazuo
AB An .alpha.-mannosidase inhibitor, mannostatin A, from Streptoverticillium verticillus var. quintum inhibited chemotactic **invasion** of mouse B16/F10 melanoma cells in the Boyden chamber **assay**. It also inhibited in vitro **invasion** of K-ras-NIH3T3 cells. Mannostatin A did not inhibit the growth of either cell line at the concn. effective to inhibit **invasion**. Addn. of mannostatin A to the

cultured B16/F10 or K-ras-NIH3T3 cells inhibited cellular .alpha.-mannosidase activity specifically. Mannostatin A-treated B16/F10 cells also showed decreased metastatic activity in vivo in C57Bl/6 mice.

L5 ANSWER 6 OF 5763 CAPLUS COPYRIGHT 2003 ACS
AN 1987:457255 CAPLUS
DN 107:57255
TI Activation of mouse macrophages for **migration inhibition** and for **tumor** cytotoxicity is mediated by interferon-.gamma. priming and triggering by various agents
SO Journal of Interferon Research (1987), 7(2), 165-71
CODEN: JIREDJ; ISSN: 0197-8357
AU Herriott, M. J.; Leu, R. W.
AB The requirements for activation of C3HeB/FeJ mouse peritoneal macrophages to mediate **migration inhibition** from capillary tubes was compared with those conditions prerequisite for nonspecific **tumor** cytotoxicity. Both in vitro **assays** for macrophage activation required a 2-stage process that involved priming by murine recombinant interferon-.gamma. (IFN-.gamma.) and triggering by subactivating concns. of bacterial lipopolysaccharide (LPS), lipid A, poly I:C, or cobra venom factor (CVF). A dose-related increase in both **migration inhibition** and **tumor** cytotoxicity was shown with increasing concns. of IFN-.gamma. (3.0-50.0 units/mL) in synergistic combination with an LPS trigger. IFN-.gamma. alone produced low levels of **migration inhibition** or **tumor** cytotoxicity that was not attributable to LPS contamination. The concns. of the agents required for direct activation or triggering of IFN-.gamma.-primed macrophages were .apprx.2-10-fold greater for **migration inhibition** than for **tumor** cytotoxicity. These results indicate that the 2-signal process of priming and triggering for mediating mouse macrophage nonspecific tumoricidal activity is also operative in **migration inhibition** from capillary tubes. Thus, under defined conditions with purified lymphokines, the **migration inhibition assay** appears to be a reliable alternate in vitro correlate of macrophage activation by IFN-.gamma..

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L8 ANSWER 3 OF 230 CAPLUS COPYRIGHT 2003 ACS
AN 1990:588996 CAPLUS
DN 113:188996
TI Monoclonal antibody and synthetic peptide inhibitors of human **tumor** cell **migration**
SO Cancer Research (1990), 50(15), 4485-96
CODEN: CNREA8; ISSN: 0008-5472
AU Yamada, Kenneth M.; Kennedy, Dorothy W.; Yamada, Susan S.; Gralnick, Harvey; Chen, Wen Tien; Akiyama, Steven K.
AB The processes of **migration** and **invasion** by human **tumor** cells are likely to involve specific cell surface receptors, such as receptors for the extracellular matrix mols. fibronectin, laminin, and collagen. This study examd. the roles of several of these receptors using a set of monoclonal antibodies directed against the .beta.1 **integrin** family, as well as a series of synthetic peptides reported to inhibit various interactions of each of these proteins with the cell surface. The most general inhibitor of **tumor** cell **migration** was found to be the anti-.beta.1 monoclonal antibody 13, which inhibited the **migration** of human HT-1080 fibrosarcoma cells, 5637 bladder carcinoma cells, VA13 viral transformants, and HCT 116 colon carcinoma cells when fibronectin was the **migration** substrate. Moreover, this antibody was particularly effective in blocking

cell **migration** on laminin, as well as **migration** within 3-dimensional collagen gels. It also inhibited in vitro invasiveness in a reconstituted basement membrane **invasion assay** (Matrigel **assay**) at concns. as low as 1 .mu.g/mL. **Integrins** of the .beta.1 class thus appear to play a central role in several types of **migration** by a variety of human **tumor** cell lines. Anti-.alpha.5 fibronectin receptor monoclonal antibody 16 also significantly inhibited **migration** on fibronectin, but not on other substrates, in 3 of the 4 cell lines. Conversely, anti-.alpha.2 monoclonal antibody F17 strikingly inhibited **migration** in 3-dimensional collagen gels, but not on other substrates, implicating the .alpha.2.beta.1 **integrin** system in **migration** of **tumor** cells within collagenous matrixes. A series of synthetic peptides previously reported to inhibit interactions of normal cells with fibronectin, laminin, and collagen were also tested as inhibitors of **tumor** cell **migration**. Peptides contg. the Arg-Gly-Asp adhesive recognition signal were partially inhibitory, but with occasional exceptions, most other peptides had no effects on **migration**. The results indicate the central importance of several specific .beta.1 **integrins** in human **tumor** cell **migration** and show the effectiveness of monoclonal antibody treatment in blocking this process in vitro.

L8 ANSWER 5 OF 230 CAPLUS COPYRIGHT 2003 ACS
AN 2001:851117 CAPLUS
DN 135:371645
TI Propanoic acid derivatives with acyclic and heterocyclic amidine and guanidine moieties, as .alpha.v.beta.3 **integrin** receptor antagonists, useful for **inhibition** of neoplasms, bone resorption, etc.
SO PCT Int. Appl., 155 pp.
CODEN: PIXXD2
IN Bandiera, Tiziano; Vianello, Paola; Cozzi, Paolo; Galvani, Arturo
AB Novel propanoic acid derivs. are **integrin** receptor antagonists or inhibitors, in particular of the .alpha.v.beta.3 **integrin** receptor. The compds. are non-peptides of formula I and their pharmaceutically acceptable salts [wherein: G = Q'NHC(:Q)NH- or heterocyclic amidines and guanidines G1-G4; Q = NH or O; Q' = H, C1-6 alk, Ph, phenyl-C1-4-alkyl; X = bond, CH2CONH, (CH2)m, (CH2)mX'; X' = O, S, NH; m = 1-4; B = CONH, CH2CONH, C2-4 alkylene or alkenylene, (CH2)mX'; A = Ph or pyridyl (un)substituted by 1-3 of halo, CF3, C1-4 alkyl, OH, and/or C1-4 alkoxy; Y = O, S, S(O), S(O)2; R = C1-6 alkyl, Ph or C5-7 monoheterocyclyl with 1-3 N/O/S atom(s) and (un)substituted by 1-3 of halo, CF3, C1-4 alkyl, OH, and/or C1-4 alkoxy; R' = H, C1-6 alkyl, C2-4 alkenyl or alkynyl, aryl, aryl-C1-4-alkyl]. The compds. are, for instance, useful for: the treatment of solid **tumors** by **inhibition** of angiogenic growth of **tumor** vessel network, thus promoting **tumor** regression; **inhibition** of metastatic spread, thus avoiding **cancer** metastases; **inhibition** of bone resorption, thus controlling osteoporosis; **inhibition** of smooth muscle cells **migration** into neointima, thus blocking restenosis after percutaneous coronary angioplasty; and the treatment of other pathol. conditions mediated by cell adhesion, cell **migration** or angiogenesis, such e.g. diabetic retinopathy, rheumatoid arthritis and inflammation. Over 380 specific compds. are claimed. For instance, the pyridine deriv. II.2CF3CO2H (PNU 277362F) was prepd. by a generalized multi-step synthetic route. When tested in .alpha.v.beta.3-vitronectin and .alpha.IIb.beta.3-fibrinogen binding **assays**, this compd. had IC50 values of 0.016 .+-.0.009 and 9.8 .+-.4.8 .mu.M, resp., showing highly selective .alpha.v.beta.3-inhibiting activity.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001087840	A1	20011122	WO 2001-EP4472	20010419

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1282602 A1 20030212 EP 2001-936253 20010419

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

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